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Sex-related differences in the morphology of rectal mucosa-associated lymphoid tissues in C57BL/6NCrSlc mice

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Summary. Sex hormones regulate gut function and mucosal immunity; however, their specific effects on the mucosa-associated lymphoid tissue (MALT) in the rectum of mammals remain unclear. Here, we aimed to investigate the influence of sex on MALT in the rectum of mammals by focusing on the rectal mucosa-associated lymphoid tissues (RMALTs) of C57BL/6NCrSlc mice. Histological analysis revealed that RMALTs were predominantly located in the lamina propria and submucosa of the rectal mucosa, with a significant sex-related difference in the distance from the anorectal junction to the first appearance of the RMALT. Despite similar RMALT numbers, females exhibited significantly larger RMALTs than males. Immunostaining revealed the presence of various immune cells, including T cells, B cells, macrophages, proliferative immune cells, lymphatic vessels, and high endothelial venules (HEVs), in RMALTs. Compared with males, females showed elevated T cell, helper T cell, and cytotoxic T-cell gene expression levels, along with high percentages of specific T-cell subsets. The factors influencing RMALT development, such as the presence of HEVs, C-X-C motif chemokine ligand 13 expression, and RMALT-containing cell proliferation, were also explored. Overall, this study revealed the detailed attributes of RMALTs, their immune cell composition, and their determinants in male and female mice, providing insights into the sex-specific characteristics of the rectal mucosal immune system.

Key words: Sex differences, Rectal mucosa-associated lymphoid tissue, C57BL/6NCrSlc, Chemokines, M cell, Goblet cell

Introduction

Sex differences in immune responses to foreign and self-antigens, including both innate and adaptive immune responses, are well documented. The interplay between early environmental exposure and the gut microbiome contributes to sex-dependent variations in immune function, thereby affecting susceptibility to autoimmune diseases, malignancies, infections, and responses to vaccines (Klein and Flanagan, 2016). Additionally, sex-related disparities influence multiple aspects of adaptive immunity across different life stages, reflecting notable differences in the thymus, which is a key organ for T cell development (Leposavić et al., 1996).

Abbreviations. B6, C57BL/6NCrSlc; CXCL9, C-X-C motif ligand 9; GALT, Gut-associated lymphoid tissue; GP2, Glycoprotein-2; HE, Hematoxylin and eosin; HEVs, High endothelial venules; IF, Immunofluorescence; Ig, Immunoglobulin; IHC, Immunohistochemistry; LF, Lymphatic follicle; LP, Lamina propria; M cell, Microfold cell; M-ILF, Mucosal-isolated lymphoid follicles; MALT, Mucosa-associated lymphoid tissue; PAS-H, Periodic acid Schiff-hematoxylin; PBS, Phosphate-buffered saline; PFA, Paraformaldehyde; PNAd, Peripheral node addressin; PPs, Peyer's patches; qPCR, Quantitative polymerase chain reaction; RMALTs, Rectal mucosa-associated lymphoid tissues; SEM, Scanning electron microscopy; SM-ILF, Submucosal-isolated lymphoid follicles; Th cells, T-helper cells; Tregs, T-regulatory cells.

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